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Sheet	1	of	7
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Com if Known

Application Number	Not Yet Known 10/518,003
Filing Date	Herewith
First Named Inventor	Daniel S. MARTIN
Art Unit	Not Yet Known 1623
Examiner Name	Not Yet Known
Attorney Docket Number	636-C-PCT-US

U. S. PATENT DOCUMENTS

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T ⁶
		Country Code ² Number ⁴ Kind Code ⁵ (If known)				
Mee	15	PCT/US01/46886	12-04-2001	Steen-Ketzer Institute for Cancer Research, et al.	PCT International Search Report	
	16	PCT/US01/46886	12-04-2001	Steen-Ketzer Institute for Cancer Research, et al.	PCT Written Opinion	
	17	PCT/US01/46886	12-04-2001	Steen-Ketzer Institute for Cancer Research, et al.	PCT International Preliminary Examination Report	
Mee	18	PCT/US03/18716	06-13-2003	Steen-Ketzer Institute for Cancer Research, et al.	PCT Notification of Transmittal of the International Search Report	
	56	PCT/US03/18716	06-13-2003	Steen-Ketzer Institute for Cancer Research, et al.	PCT International Search Report	
	57	WO 03/23014 A1	11-25-2003	Steen-Ketzer Institute for Cancer Research, et al.	PCT Published Application	

Examiner Signature	L. El Crane 	Date Considered	09/29/2005
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)		Application Number	Not Yet Known 10/518,003
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		First Named Inventor	Daniel S. MARTIN
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		Examiner Name	Not Yet Known
Sheet 2 of 7	Attorney Docket Number	636-C-PCT-US	

OTHER PRIOR ART-NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
JEC	1	Herceg Z. & Z.-Q. Wang. Failure of poly(ADP-ribose) polymerase cleavage by caspases leads to induction of necrosis and enhanced apoptosis. Mol. Cell Biol. 19:5124-5133 (1999)	
	2	Hirsch, T. et al. The apoptosis-necrosis paradox. Apoptogenic proteases activated after mitochondrial permeability transition determine the mode of cell death. Oncogene 15:1573-1581 (1997)	
	3	Geschwind, J.-F. H., et al. Novel therapy for liver cancer: direct intraarterial injection of a potent inhibitor of ATP production. Canc. Res. 62:3909-3913 (2002) (07/15/02)	
	4	Green, D.R. & Reed, J.C. Mitochondria & apoptosis. Science 281:1309-1312 (1998)	
	5	Leist, M. et al. Intracellular adenosine triphosphate (ATP) concentration: a switch in the decision between apoptosis and necrosis. J. Exp. Med. 185:1481-1486 (1997)	
	6	Lemaire, et al. Inhibition of caspase activity induces a switch from apoptosis to necrosis. FEBS Lett. 425:266-270 (1998)	
	7	Martin, D.S., et al. ATP depletion + pyrimidine depletion can markedly enhance cancer therapy: fresh insight for a new approach. Canc. Res. 60:6776-6783 (2000)	
	8	Mehmet, H., et al. Relation of impaired energy metabolism to apoptosis and necrosis following transient cerebral hypoxia-ischaemia. Cell Death Differ. 5:321-329 (1998)	
	9	Nicotera, P. & Leist, M. Energy supply and the shape of death in neurons and lymphoid cells. Cell Death Differ. 4:435-442 (1997)	
	10	Nieminen, A.-L., et al. ATP depletion rather than mitochondrial depolarization mediates hepatocyte killing after metabolic inhibition. J. Am. Phys. 267:C67-C74 (1994)	

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**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

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Sheet 3

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Application Number

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First Named Inventor

Daniel S. MARTIN

Art Unit

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Examiner Name

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Attorney Docket Number

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<i>Me</i>	11	Nord, L.D., et al. Apoptosis induced in advanced CD8F1-murine mammary tumors by the combination of PALA, MMPR and 6AN precedes tumor regression and is preceded by ATP depletion. <i>Canc. Chemo. Pharm.</i> 40:376-384 (1997)	
	12	Sane, A.-T. & Bertrand, R. Caspase inhibition in camptothecin-treated U-937 cells is coupled with a shift from apoptosis to transient G1 arrest followed by necrotic cell death. <i>Canc. Res.</i> 59:3565-3569 (1999)	
	13	Sweet, S. & Singh, G. Accumulation of human promyelocytic leukemic(HL-60) cells at two energetic cell cycle checkpoints. <i>Canc. Res.</i> 55:5164-5167 (1995)	
<i>Me</i>	14	Tsujimoto, Y. Apoptosis and necrosis: Intracellular ATP level as a determinant for cell death modes. <i>Cell Death Differ.</i> 4:429-434 (1997)	
**	19	Colofiore, J.R., Stelf, R.L., Nord, L.D., Martin, D.S., Biochemical modulation of tumor cell energy IV. Evidence for the contribution of ATP depletion to chemotherapeutically-induced tumor regression. <i>Biochem. Pharmacol.</i> ; 1995, 50(11):1943-1948, 1995.	
<i>Me</i>	20	Hageboutsos, A., Judes, G.R., Brennan, J., Green, F., Joffman, J., LaCreta, F.P., Colofiore, J., Martin, D.S., Ozols, R.F., O'Dwyer P.J., Phase I trial of fluorouracil modulation by N-phosphonacetyl-L-aspartate and 6-methylmercaptopurine ribonucleoside. <i>Cancer Chemother. Pharmacol.</i> ; 1998, 37(3):229-234.	
	21	Kelsen, D., Martin, D.S., Colofiore, J., Sawyer, R., Colt, D., A phase II trial of biochemical modulation using N-phosphonacetyl-L-aspartate, high-dose methotrexate, high-dose 5-fluorouracil, and leucovorin in patients with adenocarcinoma of unknown primary site. <i>Cancer</i> ; 1992, 70(7): 1988-1992.	
	22	Kemeny, N., Schneider, A., Martin D.S., Colofiore J, Sawyer, R.C., Derby, S., Salvia, B., Phase I trial of N-phosphonacetyl-L-aspartate, methotrexate, and 5-fluorouracil with leucovorin rescue in patients with advanced cancer. <i>Cancer Res.</i> ; 1989, 49(16): 4636-4639.	
	23	Kemeny, N.E., Schneider, A., Martin, D.S., Phase I trial of PALA, methotrexate, fluorouracil, leucovorin, and uridine rescue in patients with advanced cancer. The use of uridine to decrease fluorouracil toxicity. <i>Cancer Invest.</i> ; 1990, 8(2):263-264.	
<i>Me</i>	24	Koutcher, J.A., Alfieri, A.A., Matie, C., Meyer, K.L., Street, J.C., Martin, D.S., Effect of 6-aminonicotinamide on the pentose phosphate pathway: 31P NMR and tumor growth delay studies. <i>Magn. Reson. Med.</i> , 1996, 36(6):887-892.	

Examiner
Signature

D. E. Crane

Date
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 4

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First Named Inventor	Daniel S. MARTIN
Art Unit	Not Yet Known 1623
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Attorney Docket Number	636-C-PCT-US

OTHER PRIOR ART-NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
JEC	25	Koutcher, J.A., Alfieri, A.A., Tsai, J.C., Matei, C., Stolfi, R.L., Ballon, D., Martin, D.S., Evaluation of chemotherapy and radiation enhancement and 31P NMR spectral changes induced by biochemical modulation. Cancer Invest., 1997, 15(2)111-120.	
**	26	Koutcher, J.A., Alfieri, A.A., Thaler, H., Matei, C., Martin, D.S., Radiation enhancement by biochemical modulation and 5-fluorouracil. Int. J. Rad. Oncol.; 1997, 39(5):1145-1152.	
JEC	27	Mahmood, U., Street, J.C., Matei, C., Ballon, D., Martin, D.S., Koutcher J.A., in vivo detection by 31P NMR of pentose phosphate pathway block secondary to biochemical modulation. NMR Biomed.; 1996, 9(3):114-120.	
	28	Martin DS, Kemeny NE. 1992. Modulation of fluorouracil by N-phosphonacetyl-L-aspartate: a review. Semin. Oncol.; 19(2 Suppl 3):49-55. (March, 1992)	
	29	Martin, D.S., Kemeny, N.E., Overview of N-phosphonacetyl-L-aspartate + fluorouracil in clinical trials. Semin. Oncol.; 1992, 19(2 Suppl 3):228-233. (3/92)	
JEC	30	Martin, D.S., Stolfi, R.L., Colofiore, J.R., Nord, L.D., Sternberg, S., Biochemical modulation of tumor cell energy in vivo: II. A lower dose of Adriamycin is required and a greater antitumor activity is induced when cellular energy is depressed. Cancer Invest.; 1994, 12(3):296-307.	
88	31	Martin, D.S., Stolfi, R.L., Colofiore, J.R., Nord, L.D., Marked enhancement in vivo of paclitaxel's tumor-regressing activity by ATP-depleting modulation. Anticancer Drugs; 1996, 7(6)655-659.	
JEC	32	Martin, D.S., Schwartz, G.K., Chemotherapeutically induced DNA damage, ATP depletion, and the apoptotic biochemical cascade. Oncol. Res.; 1997, 9(1):1-5	
	33	Martin, D.S., Spriggs, D., Koutcher, J.A., A concomitant ATP-depleting strategy markedly enhances anticancer agent activity. Apoptosis; 2001, 6:125-131, 2001.	
JEC	34	Martin, D.S. Purine and pyrimidine biochemistry, and some relevant clinical and preclinical cancer chemotherapy research In: G. Powis and R.A. Prough (eds), Metabolism and Action of Anti-Cancer Drugs, 91-140. London, Taylor and Francis, 1987.	

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Sheet 5

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Filing Date	Herewith
First Named Inventor	Daniel S. MARTIN
Art Unit	Not Yet Known 1623
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OTHER PRIOR ART-NON PATENT LITERATURE DOCUMENTS

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<i>PLC</i>	35	Martin, D.S., Stolfi, R.L., Sawyer, R.C., Spiegelman, S. Casper, E.S. and Young, C.W. Therapeutic utility of utilizing low doses of N-(phosphonacetyl)-L-aspartic acid in combination with 5-fluorouracil; a murine study with clinical relevance. Cancer Res. 43:2317-2321, 1983.	
	36	Martin, D.S., Alfieri, A., Koutcher, J.A., et al., Selective-killing of drug-resistant mammary carcinomas by exploiting the tumor cell ATP-viability threshold. Proc. AACR 45:570 (Abstract 2462), 2004.	
	37	Martin, D.S., Stolfi, R.L., Colofiore, J.C., Koutcher, J.A., Alfieri, A., Sternberg, S., and Nord, L.D. Apoptosis resulting from anti-cancer agent activity in vivo is enhanced by biochemical modulation of tumor cell energy. In: M. Lavín and D. Walters (eds.) Programmed Cell Death. The Cellular and Molecular Biology of Apoptosis 279-296, New York: Harwood Academic 1993.	
	38	Martin, D.S., Stolfi, R.L., Nord, L.D. and Colofiore, J.R. Enhancement of chemotherapeutically-induced apoptosis in vivo by biochemical modulation of poly-(ADP-ribose) polymerase. Oncol. Rep. 3:317-322, 1996.	
	39	Martin, D.S. Cancer chemotherapy: past is prologue. Mt. Sinai. J. Med. 52:426-434, 1985.	
	40	Martin, D.S., Bertino, J.R., and Koutcher, J.A. ATP depletion. + pyrimidine depletion can markedly enhance cancer therapy. Fresh insight for a new approach. Cancer Res. 60:6776-6783, 2000.	
	41	Koutcher, J.A., Alfieri, A., Stolfi, R.L., Devitt, M.L., Colofiore, J.R., Nord, L.D., and Martin, D.S. Potentiation of three drug chemotherapy regimen by radiation. Cancer Res. 53:3518-3823, 1993.	
	42	Colofiore, J.R., Stolfi, R.L., Nord, L.D., and Martin, D.S. On the relationship of ATP-depletion to chemotherapeutically-induced tumor regression. Int. J. Oncol. 7:1401-1404, 1995.	
	43	Nord, L.D. Stolfi, R.L., Colofiore, J.R., Martin, D.S., Correlation of retention of tumor methylmercaptopyrimidine riboside-5'-phosphate with effectiveness in CD8F1 murine mammary tumor regression. Biochem Pharmacol; 1996, 51(5):621-627.	
<i>PLC</i>	44	Nord, L.D., Stolfi, R.L., Alfieri, A.A., Netto, G., Reuter, V., Sternberg, S.S., Colofiore, J.R., Koutcher, J.A., Martin, D.S., Apoptosis induced in advanced CD8F1-murine mammary tumors by the combination of PALA, MMPP and 6AN precedes tumor regression and is preceded by ATP depletion. Cancer Chemother. Pharmacol.; 1997, 40:376-384.	

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DEC 2002**OTHER PRIOR ART—NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
<i>See</i>	45	O'Dwyer, P.J., Judes, G.R., Colofiore, J., Walczak, J., Hoffman, J., LaCreta F.P., Comis, R.L., Martin, D.S., Ozols, R.F., Phase I trial of fluorouracil modulation by of N-phosphonacetyl-L-aspartate and 6-methylmercaptopyrine riboside: optimization of 6-methylmercaptopyrine riboside dose and schedule through biochemical analysis of sequential tumor biopsy specimens. J. Natl. Cancer Inst.; 1991, 83(17):1235-1240.	
<i>See</i>	46	Stolfi, R.L., Martin, D.S., Enhancement of anticancer activity by selective inhibition of rapidly proliferating tissues of the host. Pharmacol. Ther.; 1991, 49(1-2):43-54.	
<i>See</i>	47	Stolfi, R.L., Colofiore, J.R., Nord, L.D., Kautcher, J.A., Martin, D.S., Biochemical modulation of tumor cell energy: regression of advanced spontaneous murine breast tumors with a 5-fluorouracil-containing drug combination. Cancer Res.; 1992, 52(15):4074-4081.	
<i>See</i>	48	Stolfi, R.L., Colofiore, J.R., Nord, L.D., Martin, D.S., Enhanced antitumor activity of an Adriamycin + 5-fluorouracil combination when preceded by biochemical modulation. Anticancer Drugs; 1996, 7(1):100-104.	
	49	Jurkowitz, et al., Adenosine, Inosine, and Guanosine Protect Glial Cells During Glucose Deprivation and Mitochondrial Inhibition: Correlation Between Protection and ATP Preservation. Journal of Neurochemistry, 1998, 71(2):535-548.	
	50	Lieberthal, et al., Graded ATP depletion can cause necrosis or apoptosis of cultured mouse proximal tubular cells. American Physiological Society; 1998, F315-F327.	
	51	Lu, et al., Cellular ATP Depletion by LY309887 as a Predictor of Growth Inhibition in Human Tumor Cell Lines. Clinical Cancer Research; January 1, 2000, 5:271-277.	
	52	Venkatachalam, et al., Energy Thresholds That Determine Membrane Integrity and Injury in a Renal Epithelial Cell Line (LLC-PK1). J. Clin. Invest.; 1988, 81:745-758. (3/88)	
	53	Anundi, et al., Fructose prevents hypoxic cell death in liver. The American Journal of Physiology; 1987, Sep;253(3 Pt 1):G390-G396.	
<i>See</i>	54	Cannon, et al., The Effects of Fructose on Adenosine Triphosphate Depletion following Mitochondrial Dysfunction and Lethal Cell Injury In Isolated Rat Hepatocytes. Toxicology and Applied Pharmacology; 1991, 108(3):407-416.	

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<i>[Signature]</i>	55	Yager, et al., Correlation between Content of High-Energy Phosphates and Phypoxic-Ischemic Damage in Immature and Mature Astrocytes. Elsevier Science Publishers, Amsterdam; 1994, 82(1-2):62-68. (October 14, 1994).	

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